Claims 1 and 30 have support in the written description on page 5 line 31 to page 6 line 3. Although these lines do not provide explicit support for this added limitation, these lines do indicate that ABP-1 undergoes a receptor-type binding activity and thus it inherently lacks enzymatic activity. It is settled law that if the specification adequately defines a compound, it does not constitute new matter to amend the written description and claims to recite an inherent characteristic of the compound. See In re Magerlein and Schneider, 145 USPQ 683 (CCPA 1965) citing In re Nathan, 140 USPQ 601, 603 (CCPA 1964).

Claim 3 has been amended to incorporate the binding region of ABP-1 as a necessary limitation in the claim. Support can be found in SEQ ID Nos. 2, 3, and 4.

Claims 28-30 have been corrected as suggested by the Examiner to correct problems with multiple dependency.

Election/Restriction

The Examiner has withdrawn claims 28 and 29 from consideration by constructive election on the basis of original presentation. The withdrawal of these claims from consideration is respectfully traversed. Upon the finding of allowable subject matter, it is respectfully requested that these method claims be rejoined with the composition and compound claims in a manner that is consistent with the decision In re Ochiai, 37 USPQ2d 1127

(Fed. Cir. 1995) and as detailed in the "Guidelines for Treatment of Product and Process Claims of Chemical and Biotechnological Inventions" issued by the Commissioner of Patents on February 28, 1996.

Specification

The Applicants would like to thank the Examiner for the withdrawal of the objections to the Brief Description of the Drawings.

Rejection under 35 USC §112, first paragraph

Claims 1-8 and 31-33 have been rejected under 35 USC § 112, first paragraph for lack of enablement. Claim 3 has been amended to include the limitation that the ABP-1 variant contains the amino acid sequence of SEQ. ID No: 4. With the above amendment and the following remarks, we respectfully request that the rejection of claims 1-8 and 31-33 under 35 USC §103(a) be withdrawn.

An assertion has been made that the claims are not enabled for amino acid sequences having the indicated levels of homology. The Examiner relies on the cited article by Bork (Genome Research, 10, pp. 398-400, (2000)) as teaching the unpredictability of predicting protein function based on sequence

analysis. However, the rejection of the claims over this reference is inapposite, as it appears that Bork largely regards the unpredictability of predicting protein function from high throughput genomic sequencing, not protein sequencing and homologies. Thus, the Examiner is basing the rejection on a reference that relies on DNA sequences for predicting function and not on amino acid sequences as is claimed.

Moreover, the Examiner has correctly pointed out that post-translation modifications occur in proteins and that alternative (pre-translational) splicing may occur in DNA. This pre-translational splicing is putatively a reason why predicting protein function and structure from DNA sequencing may not be foolproof and also a reason why applying the Bork reference is inappropriate. Because an additional (potential) modification step exists in the translation of DNA to proteins, using DNA sequence homology to predict protein function is inherently less accurate than using homologous protein sequences. Because the instant invention is claiming similar functions based on homologous amino acid sequences and not on DNA sequences as appears in the Bork reference, the application of the Bork reference is improper.

Further, the instant invention's function is not based solely on the determination of sequences as appears in the Bork article. In the instant invention, the binding to plasminogen kringle domains has been well characterized. The Examiner's

attention is drawn to page 19 lines 23 to page 20 line 21 where the data shows the ability of the disclosed proteins to bind angiostatin. In particular, these lines show data identifying the angiostatin-binding domain of ABP-1 (specifically Big-3, SEQ ID NO. 4). The data show clearly that Big-3 is necessary and sufficient for exerting the binding activity of ABP-1. Therefore, as long as the ABP-1 variants possess the angiostatin binding domain, they should be able to exert their bioligical function.

Thus, in consideration of the above arguments, one skilled in the art would know how and be able to make a reasonable prediction whether a protein having $\geq$80% homology to the enumerated SEQ ID would have binding and anti-angiogenic activity, particularly when that protein has a known angiotensin-binding domain in it.

Rejection under 35 USC §102(b)

Claims 1 and 30 have been rejected under 102(b) as being anticipated by Peterson et al. (J. Biol. Chem., 205(11), pp. 6104-6111, (1990)). Claims 1 and 30 have been amended to include a proviso that the respective proteins of these claims do not cleave the plasminogen kringle domain. It is believed that this limitation is sufficient to obviate the rejection.

Peterson et al. disclose uPA and tPA which both bind the N-terminal fragment of plasminogen, thus falling within the scope of claims 1 and 30. Applicants respectfully request reconsideration and withdrawal of the rejection.

INSTANT INVENTION

The instant invention is drawn to an isolated human protein, which has been named "ABP-1", involved in angiogenesis, which acts as a receptor of the N-terminal fragment of plasminogen.

PRIOR ART

Peterson et al. (Journal of Biological Chemistry 205(11):6104-6111, 1990) disclose tPA and uPA and both proteins are components of the plasminogen activation system which are known to enzymatically convert plasminogen to plasmin by cleaving a specific peptide bond. Thus, tPA and uPA act enzymatically upon plasminogen and bind plasminogen in an enzyme active site.

DISTINCTIONS BETWEEN THE INSTANT INVENTION AND THE PRIOR ART

ABP-1 is distinct from the plasminogen-binding proteins of the prior art. ABP-1 is different from tPA and uPA as ABP-1 has no enzymatic activity on kringles 1-4 and/or 5 (angiostatin) of plasminogen. ABP-1 does not cleave any peptide bonds on plasminogen. The interaction between ABP-1 and angiostatin is of the receptor-ligand type in that it is merely a binding

interaction without a subsequent enzymatic reaction. In a sense, a "ligand-receptor" type interaction might be characterized as a binding at an allosteric site. Binding of a ligand to its receptor typically modulates an enzymatic activity of the receptor but the ligand is not acted upon by the receptor. On the other hand, an enzyme-substrate interaction is characterized by binding of the substrate at an "active site" that not only binds the substrate, but acts further upon it.

Thus, a substantial difference between the uPA and tPA enzymes of the prior art and the ABP-1 receptor of the present invention is that uPA and tPA bind plasminogen in an enzyme active site, whereas ABP-1 (and portions thereof) bind plasminogen in a ligand-receptor site. Claim 1 has been amended to recite ". . . wherein said protein does not cleave plasminogen kringle domains". As such, claim 1 is commensurate with the above argument. Therefore, the instant invention is not anticipated by Peterson et al. and we respectfully ask that the rejection of claims 1 and 30 under 35 USC §102(b) be withdrawn.

Conclusion

The Applicants wish to thank the Examiner for the indication that Claims 3-8 and 31-33 are free of the art. Because it is believed that the above amendments and remarks address all of the rejections presented by the Examiner, withdrawal of the pending

rejections are respectfully requested and a notice of allowance to that effect is earnestly solicited.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to January 19, 2001 in which to file a reply to the Office Action. The required fee of $110.00 is enclosed herewith.

If the Examiner has any questions concerning this application, he is requested to contact the undersigned at (703) 205-8000 in the Washington, D.C. area.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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